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THE RETAIL PHARMACIST AS A PURVEYOR OF PURE DRUGS *

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In a recent novel [1] which has attracted considerable attention among pharmacists is the following: "I don't see what bigger thing a man can do than to combine pure, clean, unadulterated roots and barks into medicines that will cool fevers, stop chills and purify bad blood. The doctors may be all right, but what are they going to do if we men behind the prescription case don't supply them with unadulterated drugs?" This seems like a fair question for the layman to ask and the answer to it would seem a simple one, involving only the question of honesty or integrity; but we know that the problem itself is much broader, more complicated and difficult than the writer implies, not only on account of the division of interest and responsibilities, but also on account of the inherent difficulties of the drug problem itself.

That the ideals of the reliable pharmacist are not surpassed by those of the harvester, as just quoted, is shown by an incident referred to by Professor Procter in his address to the graduating class of the Philadelphia College of Pharmacy in 1858.[2] The incident occurred in New York and related to a friend of Professor

* Read in the Symposium on Drug Standards in the Section on Pharmacology and Therapeutics of the American Medical Association, at the Sixty-Third Annual Session, held at Atlantic City, June, 1912. Reprinted from JOUR. A. M. A., Nov. 2, 1912, pp. 1599–1603.

[1] Porter, Gene Stratton: The Harvester, p. 41, Doubleday, Page & Company.

[2] Procter, William: Am. Jour. Pharm., 1858, xxx, 202.

Procter's whom he called Colton, and who at that time was a prominent pharmacist on Broadway. The pharmacist, having occasion to replenish his stock of cantharides and finding that the wholesale druggist with whom he usually dealt had none, went to another wholesale druggist whom the narrator named Haswell. When Colton entered the extensive establishment the following dialogue ensued:

Colton: "I am informed that you have powdered cantharides of good quality, and I am desirous of getting some that are reliable."

Haswell: "O, certainly! You will find none better. We had the powder made expressly for our sales from selected flies."

Colton: "I am particular in providing this drug, as you know how much depends on its efficient and prompt action."

Haswell: "You may rely on our article as in good condition."

Here the conversation closed; Colton gave his order and left the store. Some weeks after while he was engaged at his counter, Haswell walked in, evidently under some nervous excitement, and the following occurred:

Colton: "Good morning, Mr. Haswell, can I serve you to-day?"

Haswell: "A member of my family has been taken suddenly ill; her physician, among other treatment, has prescribed a blister, and I have come out of my way, believing from your well-earned reputation that we may rely on your cerate, and much depends on the rapid action of the plaster."

Colton: "I have always been careful in preparing this cerate from good flies and, fortunately, in this instance I have your own testimony, in addition, in their favor."

Haswell, who had till that moment forgotten the first transaction, quickly replied: "But, sir! Are you sure those flies were active? Have you tried them?"

Colton: "You said they were when you sold them to me."

Haswell: "But, my dear sir, this blister is for my *daughter!* Don't you understand? For my *only daughter!* Can I rely on it?"

Colton: "For your *daughter!* And so my cerate is for every other man's daughter who deals with me and may need it, and who is as dear to his affection as yours is to you. When I purchased those flies from you, it was your reiterated assurance of their reliability which chiefly induced me to take them, but now I perceive that your language had no real value and was given in the spirit of a huckster. I trust, sir, that this incident will be of use in your future transactions; and for your present comfort I may assure you that your flies were found to be efficient before they were dispensed."

Haswell acknowledged the justice of the rebuke and said that never before had he been properly impressed with the responsibility attached to the wholesale drug business.

INCREASE IN THE NUMBER OF DRUGS.

Until about twenty-five years ago the list of drugs in the Pharmacopœia represented those which were chiefly employed by the physician. At that time it was possible for the pharmacist to have a good oversight of the drugs and preparations which were employed. I can even recall when the Shakers sold directly to individual pharmacists many of the indigenous drugs that were used. While the means for the identification of drugs and chemicals were meager as given in the Pharmacopœia at that time, yet the professional pharmacist by his experience and training was enabled to judge quite well regarding the quality of drugs, his judgment depending much on their appearance, odor and taste. At that time many pharamacists handled the crude drugs described in the Pharmacopœia, and after grinding them themselves made nearly all of the pharmacopœial preparations, as these were all used in sufficient quantity to make it worth while.

Since that time drug-stores have been multiplied, pharmaceutic manufacturing houses have been established in great numbers, large chemical houses have been developed and the number of remedial agents has increased until it is safe to say that the articles in the Pharmacopœia represent but a small part of the substances actually used by the medical profession. While these changes have gone on in pharmacy we must recognize that they have reflected at the same time the changes in the practice of medicine. Such pressure has been brought to bear on physicians by the interests directly concerned that instead of their using pharmacopœial drugs and preparations we find them prescribing extensively the newer synthetics, the active principles and special preparations of manufacturers. The result of all this has been to add to the shelves of the pharmacist a host of remedies which are likely to be required at any time.

Beginning with the use of the standard fluidextract of ergot manufactured by Dr. Squibb, which was extensively designated in the prescriptions of physicians, we have seen this specialization developed and extended until to-day the pharmacist is compelled

to carry a line of official preparations made by quite a number of manufacturers. While it is true that the competition among manufacturers and the development of definite standards in the Pharmacopœia have caused the production of a line of assayed drugs and preparations which in some cases at least are superior to and more uniform than those manufactured a few years ago, yet even these preparations may deteriorate or their properties change, in some instances, depending on how long they have been kept in the stock of the manufacturer or jobber as well as on the druggist's shelf. This places a great responsibility on the retail pharmacist, as he must have exact information regarding the value of drugs and preparations at the time they are dispensed. I think it can safely be said that the professional pharmacist usually exercises a great deal of care in selecting drugs and chemicals of good quality and in the making of galenicals which will be found to be efficient by the physician. Furthermore, even with those preparations which he purchases from a manufacturer, he will usually in one way or another make sufficient tests to satisfy himself that they are true to the label, so that there probably never has been a time when the professional pharmacist was more alert and more desirous of working with the physician than at the present. At this point I wish to refer to an article by Mr. Henry C. Blair[3] which, it seems to me, is well worthy of perusal. It is a practical exposition of what a professional pharmacist is capable of doing, and as the article was prepared essentially in the interest of professional pharmacy and was published in a pharmaceutical journal it will stimulate the pharmacists of the United States to endeavor to attain even higher efficiency in the professional part of their calling. My object in mentioning this paper here is to show to physicians that there are among pharmacists those who give serious thought to the question of the purity and reliability of the medicines which they dispense.

It is probably true that there are more pharmacists in business than are necessary to supply the drugs and medicines required by the public; still the number of strictly reliable, conscientious or so-called professional pharmacists probably does not exceed the demand, and by a little inquiry physicians should have no difficulty

[3] Blair, H. C.: The Manufacture of Galenicals by the Retail Pharmacist—Its Possibilities and Limitations, Jour. Am. Pharm. Assn., 1912, i, 17.

in determining their location and thus be enabled to direct their patients to them. But of course no business alliance should exist between physicians and pharmacists in such cases. In this way the mere traders, whether doing a small or a big business, would in time become differentiated from the class of true pharmacists, even though they did call themselves druggists; and the two professions would be mutually protected to a greater degree than probably obtains at present. While some physicians might hesitate in a matter of this kind, the question is too important to be neglected, and we should not wait until there is a separation by pharmacy laws of the true apothecary or professional pharmacist from the mere vender of drugs. But laws or no laws, the most reliable pharmacist will always be the one who has the ability and conscientious scruples to take the initiative himself in keeping his stock up to standard.

Until recently, we may say, and this is particularly apparent if we turn over the pages of a book like that of Dragendorff's [4] with the thousands of remedies there recorded, our principal object in the study of medicinal substances seems largely to have been to collect in one place all the remedies that have been used, thus seeming to indicate that we were afraid of losing something that might prove ultimately useful to mankind. This period is contemporaneous in the United States with the time when the great compilations or dispensatories were popular, these being useful to the pharmacist and suggestive to the physician. Furthermore, our knowledge of drugs, apart from certain tests for identity, has consisted largely of unconfirmed statements regarding their value, so that we may say that the most useless things, like the pebbles, have been too frequently polished, while our knowledge of the most valuable drugs, like the uncut diamonds, remains bedimmed. With the exception of a comparatively few of the vegetable drugs our knowledge regarding their active principles and specific action is more or less indefinite, to say the least, and hence they are for the most part without quantitative standards, even of purity.

Owing to the fact that there are many factors which cause a variation in the constituents of drugs, such as for example those which modify the character and quantity of the constituents depending on how and when the drugs are gathered and how they

[4] Dragendorff, George: Die Heilpflanzen, 1898.

are cured or dried and subsequently handled, it becomes exceedingly difficult for the pharmacist to furnish a uniform article from time to time, particularly in cases in which there are no standards for the active remedial constituents. The difficulties of the pharmacist, dealing as he does with galenicals containing the constituents of living plants, are in a measure comparable to the difficulties of the physician who finds his patient a living organism with individual variations that preclude his determining with absolute precision the amount or character of response with any given quantity of drug. But as the medical profession is directing its attention as never before to a scientific study of the action of drugs, so the members of the pharmaceutic profession are advancing and attempting to provide drugs and preparations with a definite quantity of active principle.

FACTORS IN THE IMPROVEMENT OF DRUGS.

To give assurance of the progress that is being made I may mention some of the factors which are contributing to an improvement in the quality of drugs.

Legislation.—One of the most important of these is the enactment and enforcement of national and state laws relating to drugs and medicines. This beneficial influence has been going on ever since Congress, in 1848, passed the law requiring all imported drugs and medicinal preparations to be inspected before passing the custom-house. In the address of Professor Procter [2] already referred to he calls attention to the fact that at that time at the port of New York alone something like 100,000 pounds of spurious, adulterated and deteriorated drugs were annually rejected and screened out of the market which but for this law would have been distributed throughout the United States. I have not seen the figures showing the amount of spurious and adulterated drugs, which were refused admission into the United States since the passage of the Food and Drugs Act of 1906, but I am sure that it was quite large, as the standards adopted were not only those of the U. S. Pharmacopœia and the Association of Official Agricultural Chemists, but those representing the most recent researches in pharmaceutic chemistry and pharmacognosy. To what an extent we have progressed may be seen from the picture that Professor Procter has given us of the conditions that prevailed fifty years ago.

The power of Congress is limited to the custom-house when it presents us foreign products in good condition. Once beyond the examiner, they are opened to the mercy of American ingenuity; the skill which evidences itself in the production of *genuine* French brandies, wines and perfumes is not slow to enter the domain of medicines, and by the aid of modern alchemy transmute the bitterness of willow bark, and the glossy fibre of the cotton boll into veritable quinine of Pelletier and Caventou. Legislation to meet this evil in its home aspect, must originate and be carried into effect by the authorities of each state; adulterating medicines must be made a felony, punishable by statute, just as any other crime against the welfare of the public health. But amid the diversified interests striving for ascendency at our legislative centres, such wholesome sanitary measures have little chance for a hearing; for while even the reported approach of a pestilence or epidemic will send forth stringent mandates crippling commerce in their unsparing application of the laws of quarantine, the perennial, ever-present evils that we have pictured flourish and extend, unheeded by the fathers of the state.

Since the time to which Professor Procter referred there has been the realization of what seemed to the apothecary of fifty years ago an iridescent dream. The Food and Drugs Act of June 30, 1906, gave us for the first time a national control over the interstate as well as foreign commerce in drugs. During the last five years the act has been enforced to such an extent that Dr. Wiley [5] in his report for 1911 says of the conditions in the New York market: "Continued improvement in the crude drugs is shown. Only a small number of instances of entire substitution of foreign or inferior drugs is reported." There has also been a wholesome influence exerted in improving the quality of domestic drugs. The beneficial effect of the national Food and Drugs Act, supplemented as it is by the drug laws of the several states which have been framed after the national act, can hardly be appreciated except by those who actually handle drugs. While of course there will continue to be a certain amount of admixture or even substitution in foreign as well as domestic drugs, this being due in a measure to the lack of professional knowledge and responsibility of those who collect drugs, yet the whole commerce is being controlled by a strict inspection either at the custom-house or of the goods sold by the large drug dealers. With the seizures that have been made of a number of consignments of domestic drugs on the

[5] Wiley, H. W.: Report of the Chemist for 1911. From Annual Reports of the U. S. Department of Agriculture.

ground of their being misbranded or adulterated or both, I have no doubt that the large drug-dealers have brought sufficient pressure to bear on the collectors of crude drugs that we may feel that the time is not far distant when the subject of the collection of medical plants, at least in the United States, will be under the control of properly licensed persons. The collectors of medicinal plants should have just as much information, and if anything greater specialized information, concerning crude drugs than is expected of the dealer in crude drugs or retail pharmacists. Why shall the question of the quality of drugs be put to the retail pharmacist as a conundrum for his solution when the collector has the key to the problem? In practical metallurgy who would think of extracting thousands of tons of ore from a mine, roasting and refining it and ascertaining only in the matte or pure metal that the ore to begin with was of low grade? That this has been a common experience with regard to drugs is shown by the numerous analyses which have been published, but this condition has been greatly improved as shown by the fact that during the past year drugs of a higher grade and greater uniformity are to be found on the market.

I might add at this time that there are other encouraging signs which show us that not only is the whole commerce of drugs being brought under the surveillance of trained and scientific men in pharmacy and those who appreciate their responsibilities in this work, but also even the growing plants yielding our drugs are being brought more and more under scientific observation and control. The intelligent harvester collecting fresh drugs at the proper season may not only collect drugs that are pure and unadulterated, but also collect those that contain the maximum quantity of active constituents. This interest in the growing of medicinal plants will be found an important factor in improving the quality of vegetable drugs. While the chemical manufacturer, by improved laboratory methods, can furnish us with pure chemicals it is only by the proper study of medicinal plants in the fields that we shall ultimately secure the highest possible improvement in the quality of vegetable drugs. What has been done with plants yielding cinchona, coca, opium, zingiber, Tinnevelly senna, caryophyllus, and to some extent with the plants yielding digitalis, belladonna, and hyoscyamus is likely to be followed with a large number of other valuable drugs in the near future.

Interest in Pharmaceutic Research.—Another factor which is

affecting the quality of commercial drugs is the fact that they are being studied more intelligently than heretofore. Until recently, with few exceptions, the scientific study of drugs has been more or less superficial. At the present time greater efforts are being put forth in the study of the active principles. These studies are furthermore being supplemented by the investigations of trained pharmacologists. The result of these investigations must influence not only the practice of pharmacy, but also the practice of medicine. The empiricism of the past is being replaced with the truth of science. The researches of Power and Salway [6] (for instance) in failing to find any constituents in the seeds of the pumpkin that possess tenifugal properties, must influence not only the use of this substance by physicians, but the retention of this article by the Pharmacopœia. The numerous studies on the biochemical assay of digitalis and its preparations which have been published during the past few years and the many investigations which are still going on will shortly enable the pharmacists to supply quite uniform preparations of this important drug. Many illustrations could be given to show that our knowledge of the constituents of drugs is becoming more and more exact, and with this extension of knowledge of the active constituents we are more and more enabled to prepare galenicals which shall represent the true properties of the drug. Furthermore, this knowledge is enabling us to differentiate more clearly those drugs possessing positive medicinal action from those which are slightly efficient or altogether worthless, and by elimination of the latter to reduce the number of drugs. The sooner we can cast all positively useless drugs into the realm of the obsolete the better it will be for all concerned, except, of course, those who are desirous of adding to the number of salable commodities. These investigations, regarding the physical and chemical nature of drugs, form the basis of Pharmacopœia revision, and as the United States Pharmacopœia is the legal standard, it is at once apparent how these two factors, legislation and pharmaceutic research, are contributing most effectively to an improvement and greater uniformity in the quality of drugs of the Pharmacopœia.

Higher Standards of Education.—A third factor making for

[6] Power, F. B. and Salway, A. H.: Jour. Am. Chem. Soc., 1910, xxxii, 346.

progress in pharmacy is the higher efficiency on the part of retail pharmacists themselves. This is due to the fact that in some states a newly licensed pharmacist must show that he has had a course of instruction in a recognized college of pharmacy. There has also been a marked improvement in the curriculum of the colleges of pharmacy, so that the graduate has been pretty broadly trained and is usually quite competent to practice his profession. Furthermore, by reason of the increase in preliminary educational requirements, men and women are coming into pharmacy who are better trained and enabled to pursue their studies and take up their responsibilities with credit to their profession and satisfaction to the physician.

Not only is it true that the professional requirements are being advanced, but even the attitude of the wholesale druggists is such to-day as to convince me that they are realizing their great obligations and responsibilities as purveyors of drugs and medicines. Mr. C. Mahlon Kline,[7] in an account of the recent meeting of the National Wholesale Druggists' Association, says:

> The wholesale dealers of ten years ago were not, nor did they have to be, familiar with the professional side of pharmacy. This condition is not true to-day. The wholesaler has been compelled to assume responsibilities as to the quality of the drugs and medicines he handles, and this has driven him to interest himself in the study of drug substances; therefore, discussions having to deal with problems, standards, scientific methods of production or handling, are now heard with the greatest interest, and the purely commercial side has been forced to recede somewhat from its former preeminent position.

We know that there is a growing disposition on the part of manufacturing houses to employ competent analysts to examine drugs before they are further distributed or made into preparations. With the better output of drugs by the dealer in crude drugs and the manufacturer, and the enforcement of the national and state laws, the labors of the retail pharmacist are considerably lightened, but no one realizes better than he that he must nevertheless be alert in checking the findings of the government analysts and manufacturing houses if reliability is to be ensured in all cases.

Co-operation.—There is still another important factor contributing to the ideal practice that the professional pharmacist ever

[7] Kline, C. M.: Am. Jour. Pharm., 1912, lxxxiv, 33.

has before him and that the physician should insist on his living up to, and this is the disposition for mutual co-operation between the members of the two professions. Whatever may have been the grounds for the pessimistic attitude of physicians a decade or so ago toward the pharmaceutic calling I firmly believe that the radical changes that have been going on in pharmacy during the past few years give cause for a healthy optimism, that is, an optimism based on a belief in real progress and an earnest desire on the part of pharmacists to render the best service in their power. This does not mean that physicians shall cease to be critical, but that we shall state our criticisms with candor and fairness in joint meetings where they can be discussed and measures for improvements suggested. And here let me say that to my mind nothing augurs more for the mutual progress of therapeutics and pharmaceutical practice than those agencies which promote the coming together of the members of the two callings for discussion of the properties of drugs and their preparations as exemplified in this Section and the work of the Council on Pharmacy and Chemistry of the American Medical Association, as well as in the "get together meetings" of the local medical organizations with the various local pharmaceutic associations. In other words, if we are to make true progress we cannot well afford to be entirely independent. The words of the late Dr. Musser,[8] an honored ex-president of this Association, in a brief address which he delivered before the members of the Philadelphia College of Pharmacy, still ring in our ears and have done an incalculable amount of good in stimulating us to attain a higher goal in the practice of pharmacy. He said:

> I plead, therefore, that you make the calling of pharmacy not a profession, but a science, and that you insist that its conduct must be on the highest scientific plane to the end that those who are its devotees may be counted on, in season and out of season, as men having no code and no regulation, breathing only the spirit of doing unto others as you would be done by.

SUMMARY.

In summarizing the points that I have attempted to make in this paper, I may say that the professional pharmacist recognizes his obligations to the medical profession and the dependence which the physician has on him in the dispensing of pure drugs. Further-

[8] Musser, J. H.: Am. Jour. Pharm., 1905, lxxvii, 60.

more, in spite of their difficulties, there have been professional pharmacists who have consistently tried to handle only pure drugs and to dispense preparations which the physician would find to be efficient.

While it is true that the apothecary is dependent in some measure on the ability and integrity of the large dealer from whom he purchases his supplies, yet he attempts to check in a measure the articles distributed by the manufacturer, recognizing that he stands between the manufacturer and the patient.

Furthermore, there are fortunately a number of factors which are making it easier for the pharmacist to purchase pure drugs and dispense good preparations. These are the enactment and enforcement of drug laws, the greater interest in pharmaceutic research, the higher standards of education in pharmacy and the co-operation between physicians and pharmacists.

Finally, I may say that while the pharmacist is a purveyor of articles that sell at so much per pound or so much per ounce, the ethical standards which guide him in his practice must be as stringent and binding as those which guide the physician in his practice. And while physicians may differ as to diagnosis and as to the relative value of medicines and while every patient reacts more or less variously toward different medicines and toward the same dose of the same medicine, the standards set for the pharmacist must be those of uniformity and efficiency. The one constant in the equation must be the uniform quality of the drug. This is the position we are endeavoring to live up to in our teaching and in our practice, and we desire every possible co-operation on the part of physicians in advancing and maintaining this standard. While we sometimes feel that the medical profession has not sufficiently understood the task we have set out to perform, yet we trust that the physician will appreciate that the pharmacist realizes his responsibility and recognizes the importance of fostering the integrity of their mutual relations if the best results in the interests of the public health are to be achieved.

CANDY—CHEAP AND EXPENSIVE [1]

By Charles H. LaWall.
Chemist to the Pennsylvania State Dairy and Food Department.

The word "candy" is derived from the Orientals by whom sweetmeats and sugar have been used from the earliest times. The Hindustan *Khand* and the Arabic *quand,* as well as words of similar sound in other Eastern languages, signifies "sugar," and are traceable to the Sanskrit word *Khanda,* meaning a portion or piece. The definition of candy in its strictest sense limits it to "any confection having sugar as its basis, however prepared."

The word "confectionery," a broader term applied frequently to candy is from the Latin, *conficere,* to compound, and really embraces all food preparations of the nature of sweetmeats, pastry, etc., which have sugar as a basis or for the principal ingredient.

As the Oriental origin of the word indicates candy is an ancient food product and its early use by Eastern peoples points to an intuitive knowledge of the value and necessity of the carbohydrates as food stuffs. In the early days of the use of candy by European nations, the manufacture and sale of sweetmeats was exclusively carried on by druggists, who, we find in the year 1581 in Nuremburg, entered a protest against the encroachment upon their rights by other persons engaged in trade in a resolution containing the following:

"May it please the Honorable Council to lend ear to our complaints and in conformity therewith to see fit, in such a manner, to protect our interests, that henceforth we shall not be unduly oppressed by the physicians, and that each of us shall be enabled to enjoy the just results of his labors. The following, Honorable Sirs, forms the substance of our complaint:

1. The sale of all confections, formerly dispensed by us, has now fallen into the hands of the sugar dealer," etc.

It was manifestly impossible, of course, for pharmacists to control such a rapidly developing business and we find it carried on at present in an entirely separate manner, except for the fact that many druggists carry candy manufactured by others, as a side line, confining their manufacturing operations to such medicated confections as still survive in the materia medica of the present.

[1] Presented at the American Food Exposition, New York, October 28, 1912.

The manufacture of candy has probably reached the highest degree of perfection and the greatest magnitude in America, although in Germany and in France it is also of great importance, the French word "bon bon" (a duplication of the word "good") having been practically Anglicized and found in common everyday use among English-speaking peoples.

The competitive effort to originate new and attractive forms has caused candy to occupy a peculiar and distinctive place among food stuffs, both as to the attitude of the purchasing public and in the eyes of the law. Coloring matters, even of the permissible varieties, are required to have notice of their presence given to the consumer in the case of food stuffs in general, but in candy the addition of coloring matter is looked upon as an esthetic necessity in order to provide an attractive variety, and therefore any harmless color is permitted in confectionery where its presence is not deceptive and because it is really desired by the majority of purchasers.

In the manufacture of candy the basis is usually sugar or some related carbohydrate such as glucose. A carbohydrate is a complex chemical constituent of food stuffs in which carbon is combined with hydrogen and oxygen, the two latter elements being present in the same proportion in which they exist in water, hence the expressiveness of the word "carbohydrate." The carbohydrates form a valuable class of food stuffs including the starches, sugars and some of the fats and serve as fuels for the animal organism.

Sugar is obtainable from a number of natural sources, the most important of which are sugar cane, sugar beet, sorghum and sugar maple, the first and second sources being used for the refined sugar of commerce, the third and fourth being usually employed in the unrefined condition on account of the attractiveness of the natural flavor. Sugar is also used in candy in the unrefined form as molasses or brown sugar.

Glucose, another carbohydrate used in the manufacture of candy, is not a natural product, but is made from starch by the action of an acid which is afterward removed leaving the glucose in a pure condition. The bad reputation which glucose has acquired in the mind of the public is partly due to the fact that it was formerly manufactured and purified by methods which left it contaminated with harmful substances and also because, as in the case of oleomargarine and butter, it was not sold and used upon its own merits but was secretly employed as a cheap substitute for sugar, which it is capable of replacing to a large extent for many purposes. The name "corn

syrup," which is now legally applied to it is misinterpreted by the average purchaser to mean a syrup prepared from corn in the same way that syrup is prepared from the sugar cane. This impression is not correct and is also faulty in that the product can be equally well prepared from any other variety of starch as well as corn starch and in Germany is usually made from potato starch, in which case the name "corn syrup" would not be correctly applied. When properly made and purified, as is done at present, it is looked upon by the majority of authorities as being a wholesome food, the few who disagree on this point basing their objections upon the fact that unlike cane sugar it is not a simple carbohydrate of definite chemical composition, but is a complex mixture of several carbohydrates, of which one of the less important is comparatively indigestible.

When sugar is heated with small quantities of acids, such as are present in many fruits, or intentionally added in the shape of vinegar or cream of tartar in the manufacture of candy, it is chemically decomposed with the formation of a new substance known as invert sugar, which consists of two carbohydrates, both different from the original sugar and one of which is identical with the principal carbohydrate of glucose. This invert sugar, which is purposely formed in certain kinds of candy, possesses the same property as is possessed by glucose, of making a soft creamy mass which does not readily grain or crystallize.

When sugar is heated to a temperature high enough to partly burn or char, there is formed a substance called caramel, which possesses powerful coloring properties and which communicates a flavor which is attractive to many. When sugar is heated to a temperature short of the caramelizing point, it is modified in its character and assumes a state known as barley sugar, in which it is in a solid, glassy, uncrystallizable condition. There are other and intermediate temperatures at which sugar assumes physical conditions varying according to the degree of heat, and therefore such terms as "thread," "soft ball," "hard ball," "crack" and "hard crack" are technically used by confectioners to describe the conditions which the cooked mass will assume upon cooling. This illustrates the infinite possibilities of candy making taking into account the immense number of colors and flavors available for use, and shows how a large variety of forms and consistence may result from the use of a comparatively small number of basic ingredients.

We often hear astonishment expressed at the fact that candy

can be sold so cheaply and equal astonishment at the fact that it can be made to cost so much. Both sets of critics overlook several important facts which are easily apparent to the reasoning individual. About the cheapest price at which good candy can be sold at retail to afford even a small margin of profit, is 8 or 10 cents a pound. Such candy can be and usually is pure and wholesome, as in it are used only sugar or molasses, glucose, flavors and colors, the total cost of which to the manufacturer will not aggregate more than 6 or 7 cents a pound, and as all candy contains more moisture (added in its preparation) than is naturally present in the ingredients, another element of profit, usually overlooked, is apparent.

When we consider the higher priced candies and the causes for their high prices, we find that not only is the labor expended upon them much greater in proportion (many of them being made entirely by hand while the cheaper candies are made altogether by machinery), but that expensive ingredients such as nuts, chocolate, fruits, etc., are freely used, thus accounting for much of their increased cost.

At the present time it may be confidently stated, I believe, that candy is more rarely adulterated than ever in its history. In the Federal Food and Drugs Act of June 30, 1906, the following specific clause is directed toward candy: "A substance shall be deemed to be adulterated: In the case of confectionery: If it contains terra alba, barytes, talc, chrome yellow, or other mineral substance or poisonous color or flavor or other ingredient deleterious or detrimental to health, or any vinous, malt or spirituous liquor or compound or narcotic drug." We here see a specific prohibition of a number of substances by name. Terra alba is a synonym for powdered gypsum, a pulverized rock resembling plaster of Paris; barytes is another mineral substance, very heavy and insoluble, used principally as a filler in paper manufacture or as a white pigment; talc is powdered soapstone, the substance commonly used as a toilet powder; chrome yellow is a poisonous compound of lead used as a pigment. None of these, with the exception of talc, which has been reported in small quantities in certain candies like jelly beans where it is used as a polishing agent, has been reported as a candy adulterant for years. The manufacturers of candy themselves have, through their trade organizations, brought about a cessation of trade practices which were in vogue some years ago and which were undoubtedly harmful. Even before the publishing

of the ruling of the U. S. Department of Agriculture, in which a list of permitted colors was given, these same confectioners' associations both here and abroad, had been working toward the same end, namely, encouraging the use of a certain few colors which were known to be harmless and the discouraging of the use of a large number which were either known positively to be harmful or were of doubtful character. This is not to be taken as meaning that all candy manufacturers lived up to these rules or that no adulterated candy has been sold, for the published records of the Federal cases and the Proceedings of the many State Dairy and Food Commissioners have shown otherwise.

There have been found in candy in the past, and prosecutions have been brought and sustained against the cases, such products as sulphur dioxide, a bleaching agent formerly used extensively in glucose but now discontinued for that purpose, and also found in candy as the result of the use of impure gelatin or glue; shellac and similar waterproof glazing materials sometimes carrying with them other harmful constituents such as arsenic; alcoholic liquors, and sometimes fusel oil in cordial drops; brown mineral pigments in imitation of chocolate, and other constituents equally discreditable, but by far the greater proportion of the candy sold for some time past has been free from positively harmful ingredients.

In 1911, working under the direction of State Dairy and Food Commissioner James Foust of Pennsylvania, I made an extensive investigation of more than 250 samples of candies, particularly of the cheap varieties, and of this number only 4 cases were recommended for prosecution, 3 for the use of small quantities of talc and 1 for the use of sulphur dioxide as a bleaching agent. The detailed result of the examination of these 250 samples, together with comments thereon, were at that time published as Bulletin 216 of the Pennsylvania Department of Agriculture and observations were made of particular facts which I believe to be worthy of repetition at this time because I believe they are still applicable to trade conditions.

The criticism which can justly be brought against many cheap candies is not on account of the presence of constituents harmful in themselves, but partly on account of the careless manner in which such candy is handled and exposed for sale, thus rendering it liable to all kinds of contamination, partly on account of the indigestible character of some of the puffed up penny marshmallow specialties, and partly because by the competitive efforts of the man-

ufacturers to provide novelties, such candies as are in the form of flexible belts, necklaces, tubes, etc., or are in the form of toy doll babies, soldiers, whistles, guns or marbles. These latter are usually played with by the child before eating, with results that would make a bacteriologist hold up his hands in horror.

Prize package candies have also been observed by me in which small tokens made of poisonous metals are imbedded or are in contact with the candy itself.

Some of these needed reforms can be brought about only through the co-operation of such manufacturers as realize and accept the responsibility for the perpetuation of such discreditable conditions. Other reforms must be stimulated by the education of the vendor of cheap candies, who in the city is frequently a sidewalk merchant and who must be compelled by law if necessary to protect his customers, most of whom are unable to protect themselves by reason of their tender ages. I have seen candy sold by these vendors that was not only filthy as to external appearance but was also alive with vermin requiring a close examination for their detection.

One of the frauds that is frequently perpetrated in cheap candy is the substitution of cheaper, and frequently less digestible substances for chocolate. The manufacturer of such products protects himself by avoiding the use of the word "chocolate," either on the package or the invoice. In many instances, the retailer, though careless, is ignorant of this condition and of course the purchaser is the one eventually deceived, either with or without the connivance of the manufacturer or retailer. This condition should also be remedied. When a candy which looks like chocolate is made wholly or partly from any chocolate substitute, the same protection should be afforded the purchaser as is given in similar instances in other classes of food products.

In the more expensive candies these conditions or others of a similar character are less likely to occur. One which I call to mind is the fact that most of the crystallized violet and rose leaves which are used partly for their decorative effect in expensive box candies, are artificially colored, and that in some cases what look like candied violets are in reality selected popcorn flakes ingeniously colored and sugared to give the appearance of violet flowers.

These few facts regarding candy are herewith presented in the hope that their dissemination will lead to a more widespread interest in the matter which will ultimately result in the still further improvement in the purity and wholesomeness of candy, cheap and expensive.

RHUBARB AS A SOURCE OF COLOR IN PLACE OF GOLDEN SEAL.

By John K. Thum, Ph.G., Pharmacist at the German Hospital, Philadelphia, Pa.

Hydrastis or golden seal is frequently used for its property of imparting a golden-yellow color to liquid pharmaceutical preparations.

At the hospital with which I am connected, we have been using it for many years to give this color to our liquid antiseptic or "Listerine."

The exorbitant price demanded in recent years for this drug, makes its use altogether prohibitory for this purpose. Naturally, a substitute to take its place is desirable and one was sought for among vegetable drugs.

Rhubarb was the drug whose possibilities impressed themselves on the writer's mind and after some experimentation, was adopted for this purpose as desirable in every way.

Our method of obtaining the coloring is very simple, namely, the maceration for twenty-four hours and percolation of a definite amount of crude ground drug (3 per cent.) with alcohol to a definite volume.

This alcoholic solution can be used in varied amounts to give golden-yellow tints to any liquid preparation.

THE EDUCATIONAL WORK OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION.*

By M. I. Wilbert, Washington, D. C.

The object of this paper is to direct the attention of American Pharmacists to the work of the Council on Pharmacy and Chemistry of the American Medical Association and to call attention more particularly to the educational work that has been done in the past and the possible elaboration of this same line of work in the future.

The origin and object of the Council has been well outlined by Torald Sollmann in a series of articles entitled "The broader

* Presented at the meeting of the American Pharmaceutical Association, September, 1911.

aims of the Council on Pharmacy and Chemistry of the American Medical Association," published in the Journal of the American Medical Association and since then reprinted in the form of a pamphlet for ready reference.

The origin of the Council is also recorded in the Proceedings of the American Pharmaceutical Association for 1905 (Vol. 53, pp. 67–69), so that for the time being it will suffice to state that the Council was organized in February, 1905, for the direct purpose of investigating the then numerous and involved problems in connection with the advertising and use of proprietary remedies. As originally constituted the Council consisted of three Sub-Committees—pharmacy, chemistry, and pharmacology—with the late C. S. N. Hallberg as Secretary and "Mainspring."

The functions of the Council were primarily judicial and its first work was to assist in ridding the pages of the Journal of the American Medical Association of the advertisements of secret and semi-secret proprietary remedies.

To appreciate the really far-reaching effects of this work, more particularly the courage required to carry it on, one must compare a number of the Journal published 5 or 6 years ago with a corresponding number of to-day, and note the direct money loss in the way of "gilt edge" advertising that was involved.

At that time wiseacres on all sides predicted that the undertaking was rank folly, that the Journal of the A. M. A. could not exist without the patronage of proprietary medicine manufacturers and that the life of the Council would necessarily be a short one.

Fortunately these prophets had not taken into consideration the fact that the average American and more particularly the average American physician is willing to, and does occasionally, do some thinking for himself and usually follows his thinking up with a practical adaptation of the course that appeals to him.

While the members of the Council, individually and collectively, were maligned and abused in some quarters for being "hare-brained" destructionists, their work was appreciated and praised by the better element in American medicine and in a surprisingly short time physicians all over the country were willing to have the Council adopt much more stringent rules than the originators of the same had dared to hope for.

At a meeting of the Council held in 1908, the original ten rules were amended so as to provide for a more or less comprehensive investigation of the therapeutic claims made in connection

with patented and proprietary remedies. A fourth subcommittee, on therapeutics, was organized, and the advertising pages of the Journal were given a second overhauling, resulting, as before, in a considerable loss of revenue from advertisers of a pecuniarily reliable type, but resulting also in a corresponding increase of respectability and an augmentation in the number of subscribers showing that physicians at least are willing to learn and are capable of appreciating sacrifices for an evidently just cause.

No inconsiderable amount of the credit for the final success of the Council is due to the activity of the Chemical laboratory of the American Medical Association under the supervision of W. A. Puckner, the present secretary of the Council.

This laboratory was organized early in 1906 and the annual reports of the work done, while largely made up of reprints of articles published in the Journal are nevertheless interesting in that they present for ready reference the unusual and in many respects original chemical data involved in connection with the work of the Council.

These reports, with the "Reports of the Council on Pharmacy and Chemistry of the American Medical Association," now also reprinted annually, the "Propaganda for Reform in Proprietary Medicines" and the current number of "New and Non-official Remedies" contain a rather complete reflection of the various activities of the Council that are more fully recorded in the 8,000 or more pages of the weekly "Bulletins" circulated up to the present time.

As the total of these reports comprises upwards of 1400 printed pages it would be futile to endeavor to reflect the various accomplishments of the Council in the course of a short paper.

It may be permissible, however, to recall to your attention the work done in exposing the nature of the acetanilid mixtures, the discussion on the misuse of digestive ferments and liquid foods, and last but by no means least the exposition of the misleading claims that were made in connection with Arhovin, Somnos, Isopral, Chinosol, Probilin, Collargol, and a host of other proprietary preparations, now living or dead, which were being marketed by the manufacturers with a view of securing prompt returns on money invested in printers' ink.

Since 1908 the Council on Pharmacy and Chemistry has been increasingly active in a systematic investigation of the various problems that are involved in present-day therapeutic practices

and has busied itself with the development of plans for the systematic upbuilding of a rational materia medica by means of which it should be possible to eliminate at once and for always both therapeutic nihilism as well as therapeutic fetishism and to place therapy on a firm foundation of well-established truths.

From the very origin of the Council the members have appreciated the need for conducting an educational campaign in favor of recognized open formula or official medicaments.

The earliest efforts in this direction were undertaken by individual members of the Council through the publications of the Journal Office.

Beginning in 1905, there appeared in the Journal of the American Medical Association a series of articles entitled "The Pharmacopœia and The Physician." These articles were designed to call attention to some of the more reliable, official medicaments and to point out the advantages, to both physician and patient, that might accrue from the rational use of U. S. P. and N. F. remedies.

The articles were subsequently published in book form and have been since reprinted on two different occasions.

Early in 1906, largely through the initiative and instrumentality of the late C. S. N. Hallberg, the American Medical Association published an epitome of the U. S. P. and N. F. under the title, "Manual of the U. S. Pharmacopœia and the National Formulary."

This latter publication proved to be the immediate incentive for the now widespread U. S. P. and N. F. Propaganda that has done so much to direct the attention of retail druggists to the possibility of improving their own standing in the community by developing the professional side of their calling.

Following the publication of these books an effort was made, through a special committee, to induce teachers of materia medica to devote much if not all of their time to the discussion of well-established official medicaments so as to give to future generations of medical men a thorough grounding in the possible uses and limitations of the more important articles in our materia medica.

While this work has not been entirely futile the practical results have not been commensurate with the time and money that has been expended. The reasons for this apparent failure are directly traceable to the redundancy of the present official standards for drugs and medicinal preparations and the ever-threatening possibility of having one of the members of the State Board of

Medical Examiners propound a question regarding the possible uses and action of some little known or practically obsolete drug.

This latter obstacle is now in a fair way of being overcome and with the co-operation of the several state boards and the teachers of materia medica and therapeutics the Council has reasonable hopes of being able to issue a list of reliable medicaments to which systematic instruction in materia medica can largely be confined.

This then leads up to the most recent and perhaps the most important piece of investigative work as yet undertaken by the Council; a systematic review and study of the mooted points in drug therapy. While it is true that here the individual problems are legion it is nevertheless expected that many of them can be satisfactorily studied in a reasonably short period of time and that this work once thoroughly established will be taken up and continued by individual investigation and by other medical investigators.

It is not expected to revolutionize the materia medica of the country in any given period of time but it is expected that a systematic and conscientious investigation of the truth or falsity of certain statements made in connection with more or less well-established remedies will serve to put the practice of drug therapy on a foundation against which the "isms" and "pathies" of the future will rail in vain.

The program, as outlined, is broad enough for all who are interested in the development of scientific medicine to participate in and it is to be sincerely hoped that the members of the American Pharmaceutical Association both individually as well as collectively will lend their aid in clearing up some of the many perplexing questions in connection with the origin, composition and uses of well-established drugs.

THE FUTURE OF PHARMACY IN RELATION TO THE MODERN DEVELOPMENT OF MEDICINE.

By William G. Toplis.

The year eighteen hundred and eighty-one, is destined to become known in Medical and Pharmaceutical History, as the beginning of the most revolutionary epoch, in all of the experience of those branches of endeavor. That year brought forth a discovery whose importance is not yet generally recognized. Not

alone is it concerned with Medicine and Pharmacy, but it has performed a most important service in engineering projects of world-wide importance. It may be truthfully said, that this discovery and those it led up to, made possible the building of the Panama Canal. It was a most important factor in bringing victory to Japan and defeat to Russia. It is banishing pestilence from its breeding places everywhere, and no department of life, either animal or vegetable is beyond its influence. It has placed the practice of medicine upon a scientific basis, and inaugurated the era of preventive medicine. The day of curative measures, with which we are most familiar, is passing. In most of the cities and large communities of the world, Public Hygiene has become a very important department of government. Observe our own city of Philadelphia, we have here the largest water purification plant in existence. Its effect, in that city, is to reduce the number of typhoid fever cases, eighty per cent. of the former total, and perhaps one hundred per cent. of the water bore typhoid, peculiar to the Philadelphia water supply. A case of typhoid fever commonly runs three months. In money it is worth from fifty to one hundred dollars to the attending physician, perhaps half of that to the druggist. A similar change has taken place concerning diphtheria. Antitoxin and treatment are supplied to the patient at the expense of the communities in by far the greater number of cases. Smallpox is practically unknown, for similar reasons. Bacterins as prophylactic measures against typhoid, and a number of other diseases, are coming into increased usefulness.

Chemo-Therapy.

The latest advance has done astounding things. With one treatment of 606, Salvarsan, specific disease disappears to return no more. At least it seems so at this early date. Much is promised from the same source in the eradication of cancer. Leprosy, incurable, from remote antiquity, seems about to succumb to the new enlightenment.

The extermination of tuberculosis is within hailing distance. And so on through the whole catalogue of ills that plagued the people, unrestrained, less than thirty years ago.

The transcendental discovery by Dr. Koch, that has made possible all of these wonders and many others beside and others yet to come, is the simple fact that microscopic organisms grow

in pure culture, upon a piece of boiled potato. This is the cornerstone upon which has been built the whole science of modern bacteriology. With these facts confronting us and others of like nature to follow, we naturally turn to inquire what effect these changes are likely to exert upon the practice of Pharmacy.

Every pharmacist has observed the greatly increased development of the commercial side of the drug business as compared with its scientific side, which rather seems to be accorded to secondary place in the conduct of its affairs, regardless of the fact that this feature is the one that gives it character, and the only one that distinguishes it from ordinary merchandising.

Thirty years ago the physicians whom we knew were high-minded, dignified gentlemen, who held the ethics of their profession in such esteem that they scorned to violate them. We could not imagine any of those, passing out a handful of tablets to an office patient for a fifty cent fee. And yet the man of to-day who practices medicine under such conditions is to be condemned, no more than his predecessors are to be commended, because each of them is a product of the conditions of his day. Truly the change is to be deplored and the remedy is not yet ready. Thus we have a dreary spectacle, the most noble calling on God's green footstool, degraded through its commercial side, into a mad competition for existence. There are some other causes, beside those noted that contribute to the same effect such as increased numbers of individuals practicing both medicine and pharmacy. The latter causes, however, are self-limiting and not necessarily fatal, to the calling as a business proposition, where as with preventive measures well established, it is plain to all that both the practice of medicine and pharmacy as now conducted, come to their end. This does not mean that both doctors and druggists will disappear completely, but it certainly means that a new order of things is upon the threshold.

This is the year nineteen hundred and thirteen. Between the years 1922 and 1932, we may expect to have established a National Board of Health, with a chief officer in the cabinet and an organization similar to that of the Army, and in which every physician and every Pharmacist will be an officer of the United States Government. Those physicians, under the new order who remain in the office awaiting the call of the sick will be comparatively few in number. The remainder will be out in the broad domain of practical hygiene, every factory, farm, field, forest, stream, mine, and

what not, will then come under the watchful eye of this new army and with all of the wisdom of science, it will guard the health of the country, if any thing, more jealously than it is guarded against foreign foes. Every occupational disease will be banished, every case of communicable disease will be promptly isolated.

The men who are to perform this service will be the doctors and druggists of to-day who survive at that time, together with those who shall be hereafter graduated in those professions. Not that all of these men are at present fitted for this work, but their training and experience makes them the most available. They will, however, be subject to periodic examinations that shall determine their advance and pay, and each one will gravitate into the place that best suits his capacity. The pay of these men will be suitable to the dignity of their calling, certainly not less than that of a lieutenant in the United States Army. Under this new order the people will receive their medicine and medical treatment upon the same plan that they now receive their public school education. To the incredulous, it may be said that the people of Philadelphia alone spend annually fifteen millions of dollars for medical treatment, and medicine. Under the new system the cost would be less than half of that sum, and the people will receive better attention than at present.

Schools of medicine and pharmacy will be government institutions, such as West Point and Annapolis, and their various laboratories will be the main centres from which the operations of this Hygienic Army shall be directed.

To the incredulous, again, it may be said, these conditions are coming not because they are being sought, nor even desired, but they will be thrust upon us through the force of economic necessity.

DIGITALIS GLUCOSIDES AND ALLIED DRUGS.*

I. General and Historical.

Since the introduction of digitalis leaves into therapeutics by Withering of Birmingham in 1775, digitalis has become an indispensable drug in our materia medica. But in spite of many efforts it has yet been impossible to isolate from this drug a uniformly

* Reprinted from E. Merck's Annual Report, Vol. xxv, 1911, pp. 31 to 53.

active substance, which could fully replace digitalis leaves and supplant them in our list of most important remedies. However, the work of Homolle,[1] Quevenne,[2] Walz,[3] Nativelle,[4] Schmiedeberg[5] and Kiliani[6] has led to the isolation of a number of digitalis glucosides, several of which are much valued in therapeutics.

From the work of the above named authors it is apparent that the digitalis plant contains several glucosides, the physiological action of which varies considerably, both qualitatively and quantitatively. Therefore, before entering upon a consideration of the practical employment of digitalis and of its glucosides, the latter must be examined more closely with regard to their chemical composition and their physiological action. This is imperative for the reason that the nomenclature adopted by different authors in the literature on this subject has led to such confusion as is scarcely met with in any other field of pharmacy or pharmacology.

The first digitalis glucoside to attain any degree of importance in therapeutics was digitalin, prepared by Homolle (1845) from the leaves of *Digitalis purpurea*. Until that time all attempts to isolate an active principle from digitalis had been unsuccessful. Thus Bonjean[7] in 1843, only two years before the publication of Homolle's work, mistook a resinous body for the active substance of digitalis. Homolle himself enumerates the following as his predecessors in the field of research regarding digitalis: Bidault, Planavia, Leroyer, Rein, Haase, Welding, Dulong, Henry, Quevenne, and Tromsdorff. Homolle's method for preparing his digitalin was that formerly much in vogue for the isolation of glucoside-like vegetable substances. This method consisted in clearing the aqueous extract of the drug with subacetate of lead, and after separation

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[1] Homolle, Journal de pharmacie et de chimie 1845, I, p. 57.

[2] Homolle-Quevenne, Neues Repertorium für Pharmazie, Vol. 9, p. 2. Gazette des hôpitaux, 1850, p. 53. Union médicale, 1851, p. 69.

[3] Walz, Jahrbuch für praktische Pharmazie, Vol. 14, p. 20; Vol. 21, p. 29, Vol. 24, p. 86.

[4] Nativelle, Journal de pharmacie et de chimie 1869, I, p. 255; 1872, II, p. 430; 1874, II, p. 81.

[5] Schmiedeberg, Archiv für experimentelle Pathologie und Pharmakologie 1875, p. 16.—Neues Repertorium der Pharmazie, Vol. 24, p. 89.

[6] Kiliani, Archiv der Pharmazie 1892, p. 250; 1896, p. 273, 481; 1897, p. 425; Berichte der deutschen chemischen Gesellschaft Berlin, 1890, p. 1555; 1891, p. 339 and 3951; 1898, p. 2454; 1899, p. 2196 and 2201.

[7] Bonjean, Journal de pharmacie et de chimie 1843, p. 23.

from the lead, precipitating with tannic acid; the combination of gluocoside and tannin thus formed was decomposed by adding lead oxide, and the glucoside thus set free was then extracted with alcohol. After the evaporation of the alcohol, impure digitalin remained, this was then freed from fat by means of ether, rendered colorless by animal charcoal and then precipitated from alcohol. The preparation thus obtained consisted of both amorphous and crystalline substances, for which reason the digitalin of Homolle has been described in the literature sometimes as an amorphous and sometimes as a crystalline body. The French pharmacopœia of 1866 retained the method of preparing digitalin as described by Homolle; but this yielded a preparation which was not completely soluble in chloroform. For this reason the pharmacopœia in question required that the digitalin should be redissolved in chloroform and the latter evaporated. In this way "digitaline chloroformique" was obtained as a yellowish-brown, amorphous preparation, completely soluble in alcohol and in chloroform.

Digitalin was now further investigated by Homolle in conjunction with Quevenne, and they succeeded in isolating three different substances from digitalin. By treating it with a mixture of alcohol and ether of specific gravity 0.78, these authors obtained an insoluble residue and a solution. The former they named "le digitalin." The solution in alcohol and ether, when evaporated, left a residue which was only partially soluble in alcohol (50 p. c.). They named the soluble portion "la digitaline," and the insoluble portion "digitalose."

It may be here mentioned that Homolle's further researches, and the nomenclature adopted by him, already introduced a considerable degree of confusion, for the author unfortunately made a distinction between digitalin and digitaline. I shall therefore in the following remarks always add the name of the author, when necessary, in order to avoid errors.

Two years after Homolle's first publication regarding digitalin, Walz began his reports dealing with his work on this subject. He first prepared an alcoholic extract of digitalis leaves and precipitated those substances which were soluble in water (e. g., its aqueous extract) with tannic acid. When decomposed by lead oxide the tannin compound thus formed constituted the raw digitalin Walz. According to Walz, when this substance is treated with ether, fat and two other substances dissolve; the author named

these " digitaloin " and " digitalacrin α and β." The residue, which was insoluble in ether, was extracted with water, whereby " digitaletin " remained and " digitalin Walz " dissolved. Walz describes his digitalin as a yellowish, amorphous substance, which is distinguished from the digitalin of Homolle by being soluble in water and only with difficulty soluble in chloroform. The digitalin of Walz formerly also bore the name of " German digitalin," but it should be noted that it is not identical with the digitalinum Germanicum at present on the market, as the latter is prepared from digitalis seeds. However, Walz in the course of his studies on digitalin altered his method of preparation, and later (Cf. Canstatt's Jahresbericht 1850, Vol. 10, p. 22) he describes his digitalin as a crystalline body, very similar to the digitalin of Homolle, soluble with difficulty in water and melting at 175°.

Nativelle isolated three substances from digitalis leaves, namely digitalein Nativelle, a glucoside soluble in water, prepared by extraction with water and subsequent purification, and digitalin Nativelle, (digitaline cristallisée), soluble in alcohol and chloroform, obtained by extraction with alcohol, and thirdly digitin Nativelle, soluble in alcohol and practically insoluble in chloroform; this substance, on account of its physiological inactivity, he at first named " substance cristallisée inerte."

Schmiedeberg obtained from digitalis leaves the first preparation of digitalis which had well defined chemical characteristics and was physiologically active, viz., digitoxin Schmiedeberg; he first extracted the drug with water and then with alcohol (50 p. c.), the alcoholic extract was cleared with lead acetate, and after removing the lead which had dissolved, evaporated the solution to dryness, and extracted the residue with chloroform and distilled off the chloroform. After purifying the residue with ether and animal charcoal, as well as recrystallising it several times from alcohol, he obtained a pure hydrated preparation, melting at 145° C. For anhydrous digitoxin he gave the empirical formula $C_{21} H_{32} O_7$. Digitoxin Schmiedeberg is now simply called " digitoxin." Kiliani, who has made an exhaustive study of digitoxin and its decomposition products found that this glucoside corresponded to the formula $C_{34} H_{54} O_{11}$, and on hydrolysis yielded digitoxigenin and digitoxose. It forms white crystals, which are readily soluble in alcohol and chloroform, but only with difficulty soluble in water and ether.

Kiliani found another glucoside in digitalis leaves. This is a crystalline body, similar to digitoxin, which Kiliani named "digitophyllin." He states that its formula is $C_{32}H_{52}O_{10}$ and its melting point 231° C.

The researches of Schmiedeberg and Kiliani also yielded another body with definite chemical characteristics, viz., digitonin, with the formula $C_{54}H_{92}O_{28}$ [8] which decomposes at a temperature above 235° C. without having a well defined melting point. It is practically insoluble in water, ether and chloroform, it is more readily soluble in alcohol (80–85 p. c.). It is preferable to call this body digitonin Kiliani, because digitonin Schmiedeberg, according to Kiliani, did not represent a pure, uniform substance. Schmiedeberg described his digitonin as an amorphous substance readily soluble in water. Kiliani succeeded in demonstrating that digitonin could be obtained in either an amorphous or a crystalline form, according to the concentration of the alcohol used in the process of recrystallisation. On examination the amorphous preparation was found to be readily soluble in water, while the crystalline body dissolved with difficulty. Kraft [9] considers the digitonins described by Schmiedeberg and Kiliani to be distinct substances and would like to see the name digitsaponin introduced for digitonin Schmiedeberg. While Kiliani formerly (Archiv. der Pharmazie 1892, p. 250) assumed that digitonin was present in both the leaves and the seeds of digitalis, it is stated in his later communications (Archiv der Pharm. 1895, p. 311) that it is only found in the seeds. Kraft states that a body is present in the leaves which can be distinguished from digitonin by its melting point (260–265° C.), its solubility and its behaviour towards cholesterin. Digitonin was isolated by Schmiedeberg and Kiliani, from digitalinum Germanicum. According to Kiliani, when heated with dilute hydrochloric acid it splits up into digitogenin, dextrose and galactose. (Berichte der deutschen chemischen Gesellschaft Berlin 1891, p. 341).

Schmiedeberg also obtained from digitalinum Germanicum an amorphous digitalin with the formula $(C_5H_8O_2)n$, the chemical individuality of which, in spite of its amorphous constitution, was

[8] See Berichte der deutschen chemischen Gesellschaft Berlin Vol. 32, p. 339 and Vol. 42, p. 239. Note 6.

[9] Kraft, Schweizer Wochenschrift für Chemie und Pharmazie, 1911, p. 175. and 237.

confirmed by Kiliani. Digitalin Schmiedeberg forms a white mass, readily soluble in alcohol, hot dilute acetic acid and a mixture of alcohol and chloroform, but is only slightly soluble in cold water, chloroform and ether. When split up by acids it forms digitaliresin and glucose. On preparing his digitalin, Schmiedeberg found another glucoside soluble in water, digitalein Schmiedeberg; when treated with acids it is decomposed into glucose and a body probably identical with digitaliresin.

Digitalin Schmiedeberg and digitalein Schmiedeberg were examined more minutely by Kiliani. He was able to prove that pure digitalin, for the preparation of which he worked out an exact formula,[10] forms an amorphous white powder, which swells up in water at ordinary temperature and is soluble 1 in 1000 of water. Moreover, it is said to dissolve in 50 parts of alcohol (50 p. c.) and more readily in hot alcohol. On heating it remains white up to 200° C., begins to sinter at 210° C. and melts at about 217° C. Kiliani gave it the formula $(C_5 H_8 O_2)_7 = C_{35} H_{56} O_{14}$, but also mentions that it may have the formula $C_{36} H_{58} O_{14}$. According to Kiliani, on heating with dilute alcoholic hydrochloric acid it splits up into digitaligenin, glucose and digitalose. (Archiv der Pharmazie 1892, p. 250.)

Kiliani at first doubted the chemical individuality of the digitalein of Schmiedeberg. Keller[11] and Houdas[12] also took it to be digitonin. But Kiliani proved later that the seeds and leaves of digitalis contain a cardiac poison, soluble in water, which contains no digitalin, the physiological activity of which, therefore, precludes its identity with digitonin. Kiliani and Windaus[13] suspected the presence of a lactone in digitalein, because its neutral aqueous solution gives an acid reaction on standing. This proves digitalein to be a distinct substance, of uniform composition. Kraft,[14] on the other hand, accepts the nomenclature of digitalein only as a generic term for all the active glucosides which are soluble in water and are present in digitalis. He also places in this class gitalin, an amorphous glucoside, melting at 150–155° C., which he

[10] Archiv der Pharmazie 1892, Vol. 230, p. 252 and 1895, Vol. 233, p. 299.
[11] Keller, Berichte der chemischen Gesellschaft Berlin 1897, p. 125.
[12] Houdas, Comptes rendus 1891, p. 648.
[13] Kiliani-Windaus, Archiv der Pharmazie 1899, p. 458.
[14] Kraft, Schweizer Wochenschrift für Chemie und Pharmazie, 1911, p. 162 and 173.

isolated from digitalis leaves. It is more readily soluble in cold (1:600) than in hot water. For this reason it is partially precipitated on heating the solution, and at the same time the glucoside is decomposed. In chloroform it is soluble without alteration in all proportions. If gitalin is dissolved at ordinary temperature in 1.5 parts of alcohol and 0.75 parts of water are added, on shaking the mixture gitalin hydrate will separate. This melts at 75° C., and is only slightly soluble in alcohol and water (1:3000). On evaporating the alcoholic solution of gitalin, anhydrogitalin is formed; it appears at first chiefly as an amorphous body, but on recrystallisation from alcohol it can be obtained in crystals melting at 255° C. Gitalin, and also anhydrogitalin, give a permanent violet color with Kiliani's reagent, similar to digitalinum verum. With Keller's "layering" test gitalin gives an indigo color with the glacial acetic acid and a violet ring at the juncture of the glacial acetic acid and the sulphuric acid.

Digitalinum Germanicum,[15] obtained from digitalis seeds, is essentially a mixture of digitalin Schmiedeberg, digitonin and digitalein. It dissolves in water and alcohol, but is practically insoluble in chloroform. (Kiliani, Archiv der Pharmazie, 1895, 299.)

In order to obtain a clearer view of the subject, those substances of digitalis with which we have already become acquainted, their synonyms and their derivatives are enumerated[16] in the following remarks and briefly dealt with on the basis of the considerations mentioned above or contained in the literature:

Acrodigitalins are, according to Ludwig, those digitalis substances which do not possess the characteristics of glucosides. (Archiv der Pharmazie, Vol. 194, p. 213.)

Anhydrodigitoxigenin is obtained by the action of concentrated hydrochloric acid on digitoxigenin in alcoholic solution. It crystallises in colorless prisms corresponding to the formula

[15] According to J. Pereira (Handbuch der Heilmittellehre, translated by R. Buchheim Vol. 2, p. 293), the seeds of Digitalis purpurea were used medicinally in England, as well as digitalis leaves, in the first half of the 19th century, as they were considered more constant in their action than the leaves. The first examination of the seeds for digitalis was undertaken by A. Buchner (Buchner's Repertorium für Pharmazie, 1851, Vol. 9, p. 38.—Canstatts Jahresberichte 1851, N. F. 1. Jahrgang p. 44.)

[16] In the following decription a few special preparations containing digitalis substances are mentioned, as their names resemble the word digitalis.

$C_{22}H_{30}O_3$ (Kiliani, Berichte der deutschen chemischen Gessellschaft, Berlin 1898, p. 2458.)

Anhydrodigitic acid, $C_{10}H_{14}O_3$, occurs in two isomeric modifications, α-acid and β-acid. The α-acid is formed from digitic acid by the action of dehydrating agents. It loses its water of crystallisation at 140° C. and melts at 170° C. The β-acid melts at 263° C. (Kiliani, Archiv der Pharmazie 1894, p. 334.)

Anhydrogitaligenin, according to Kraft, is formed during the hydrolysis of anhydrogitalin, together with digitoxose and a non-crystalline sugar. It crystallises from alcohol, melts at 119° C., and gives a deep violet coloration with Kiliani's reagent. (Schweizer Wochenschrift für Chemie und Pharmazie 1911, p. 173.)

Anhydrogitalin is a product of decomposition of gitalin *q. v.*

Desoxydigitogenic acid, $C_{28}H_{42}O_9$, is obtained by the reduction of digitogenic acid by means of sodium amalgam. (Kiliani, Archiv der Pharmazie 1893, p. 448. Berichte der deutschen chemischen Gesellschaft Berlin 1899, p. 2201.)

Digalen, see digitoxin solubile Cloetta.

Digitalacrin (α- and β-) are components of raw digitalin Walz (cf. page 29).

Digitalein Nativelle was described by Nativelle as a physiologically active glucoside, soluble in water and obtained from digitalis leaves. (Moniteur scientifique 1874, p. 822. — Houdas, Comptes rendus de l'académie des sciences, Vol. 113, p. 648.)

Digitalein Schmiedeberg is a glucoside soluble in water. For details see page 31. (Archiv für experimentelle Pathologie 1875, Vol. 3, p. 33. — Houdas, Comptes rendus de l'académie des sciences, Vol. 113, p. 648. — Kiliani, Berichte der deutschen chemischen Gesellschaft Berlin 1891, p. 3950, and Archiv der Pharmazie 1899, p. 458. Keller, Berichte der deutschen pharmazeutischen Gesellschaft 1897, p. 125.)

Digitaléine Buignet represented the glucosides of digitalis leaves which were soluble in water. (Journal de pharmacie et de chimie 1872, I, p. 191.)

Digitalen is a special preparation for therapeutic use, viz., a solution of digitalis glucosides containing glycerin. (Lüders, Chemische Industrie 1905, p. 261.)

Digitaletin is a product of decomposition of digitalin Walz and is formed from the latter together with sugar by the action

of hydrochloric acid. (Compare Roscoe and Schorlemmer, Lehrbuch der organischen Chemie 1901, part 6, p. 682.) The portion of raw digitalin Walz insoluble in ether and water was also included under the name of digitaletin. (Conf. p. 29.)

Digitalicrin, according to Wiggers (Canstatt's Annual Reports 1850, Vol. 10, p. 23), is a constituent of digitalin Walz (raw digitalin), a substance with an acrid and harsh taste, of the formula $C_{11} H_{20} O_3$.

Digitalid, digitalidine and digitalosin are substances which Homolle, in his later publications, states that he found in the leaves of digitalis besides his digitalin. (Roscoe and Schorlemmer, Lehrbuch der organischen Chemie 1901, part 6, p. 682.)

Digitaligenin is a crystalline body corresponding to the formula $C_{22} H_{30} O_3$, melting at about 211° C., and formed in the decomposition of digitalin Kiliani. This preparation is soluble in alcohol and insoluble in water, and is said to have no physiological action. (Kiliani, Archiv der Pharmazie 1892, p. 250. Berichte der deutschen chemischen Gesellschaft Berlin 1898, p. 2454.)

Digitalin with no other specification is a vague term, and should be avoided in the literature and in practice in order to eliminate a source of errors and of confusion. The same applies to digitalinum and digitaline.

Digitalin, amorphous. This designation is probably chiefly intended to cover digitalinum Gallicum (digitaline chloroformique) of the French pharmacopœias of 1866 and 1895, a substance which is completely soluble in chloroform. But it must be remembered that digitalinum verum and digitalinum Germanicum are also amorphous.

Digitalin(um) crystallisatum has so far been used as a synonymous term for digitonin. As this is misleading it would be better to avoid its use altogether. In commerce, however, names which have once been introduced are difficult to get rid of. Kiliani objected to the term "digitalin cryst." as early as 1891. (Berichte der deutschen chemischen Gesellschaft Berlin 1891, p. 3953.)

Digitalin Henry was a mixture of glucosides from digitalis leaves. (Journal de pharmacie et de chimie 1845, I, p. 460.)

Digitalin Homolle is a mixture of glucosides and their products of decomposition contained in digitalis leaves, and is practically insoluble in water. (Conf. p. 28.)

Digitalin Homolle-Quevenne is the constituent of digitalin Homolle which is insoluble in a mixture of alcohol and ether. (Compare above.)

Digitalin Kiliani is identical with digitalinum verum, *q. v.*

Digitalin Lancelot was a mixture of amorphous digitalis glucosides, which was prepared from digitalis leaves according to the directions given by Lancelot. (Die Pflanzenstoffe von Husemann und Hilger, 2nd edition, p. 1234.)

Digitalin Lebourdais was a crystalline preparation obtained from digitalis leaves. (Annales de chimie et de physique, 3rd series, Vol. 24, p. 58.)

Digitalin Nativelle is a crystalline product prepared from digitalis leaves, which is probably not unlike digitoxin in constitution. According to Schmiedeberg and Kiliani, it is a mixture of several substances. (Berichte der deutschen chemischen Gesellschaft 1891, p. 3951, 1898, p. 2462.) Compare also p. 33 and Berichte der deutschen chemischen Gesellschaft Berlin 1898, p. 2454. — Journal de pharmacie et de chimie 1874, II, p. 81.

Digitalin Schmiedeberg is a chemically uniform, amorphous body of the formula $(C_5 H_8 O_2)_7$. (Archiv für experimentelle Pathologie 1875, p. 16.)

Digitalin Walz was a mixture of glucosides from digitalis leaves (compare above). (Delffs, Neues Jahrbuch für Pharmazie 1858, p. 25 [vol. 9]. — Wittstein, Wittsteins Vierteljahresschriften für praktische Pharmazie 1865, Vol. 14, p. 76.)

"La digitaline" is digitalin Homolle or Homolle-Quevenne.

Digitaline amorphe chloroformique is digitalinum Gallicum amorph.

Digitaline amorphe française is digitalinum Gallicum amorph.

Digitaline chloroformique is digitalinum Gallicum amorph.

Digitaline pharmacopée française 1884 is digitalinum Gallicum amorph.

Digitaline cristallisée is either digitalin Nativelle or digitoxin. Formerly it also applied to digitonin.

Digitaline cristallisée Pharmacopée française 1908 is identical with digitoxine Pharmacopée franç. 1908. Conf. Digitoxine Pharm. franç.)

Digitaline cristallisée française is digitalin Nativelle.

Digitaline française is digitalinum Gallicum amorph.

Digitaline Homolle-Quevenne is the constituent of digitalin Homolle which is soluble in a mixture of alcohol and ether and in

dilute alcohol, but is not identical with digitalin Homolle-Quevenne, which is insoluble in a mixture of alcohol and ether.

Digitaline Kosmann was a crystalline preparation which Kosmann extracted from the lead precipitate obtained in the preparation of digitalin Homolle. (Journal de connaissance médicale pratique 1845, Vol. 13, p. 67.)

Digitaline passive was the name which Nativelle at first gave to his digitin.

Digitaline Pharmacopée Belge II. is digitalinum Gallicum amorph.

Digitalinic acid (acid digitalinique) was the name given by Kosmann to a body corresponding to the formula $C_{22}H_{35}O_{12}$, and obtained by heating digitalin Kosmann with caustic soda. (Journal de pharmacie et de chimie 1860, II, 15. Homolle, Union médicale 1872, p. 80.)

Digitalic acid Morin is a substance obtained from digitalis leaves. Morin prepared a volatile acid by submitting digitalis leaves to steam distillation and called it "antirrhinic acid" (most probably identical with valerianic acid). He describes it as a colorless, oily mass, soluble in alcohol, but insoluble in water; it dissolves very gradually in water, with which it forms a hydrate. It possesses a characteristic smell and taste. (Journal de pharmacie et de chimie 1845, I, p. 294.)

Digitalinum fluidum was the name given by Engelhardt to a liquid, volatile, oily substance obtained from digitalis leaves, and which he regarded as the active component of digitalis. Zeitschrift für Chemie und Pharmazie 1862, p. 722.)

Digitalinum Pharmacopée française 1908 is identical with digitoxine Pharm. franç., *q. v.*

Digitalinum Gallicum amorph. is obtained from digitalis leaves according to the method given in the Pharmacopée française 1884. It also bears the name of "digitaline chloroformique." It is completely soluble in chloroform and practically insoluble in water. (Conf. p. 29.)

Digitalinum Gallicum crystallisatum is either digitalin Nativelle or digitoxine pharm. franç. 1908.

Digitalinum Germanicum is an amorphous product obtained from digitalis seeds, and is soluble in water. It consists principally of digitalinum verum, digitalein and digitonin. It was examined in detail by Schmiedeberg and Kiliani. (Archiv für

experimentelle Pathologie 1875, p. 16. — Berichte der deutschen chemischen Gesellschaft 1890, p. 1555.)

Digitalinum passivum was the name given by Nativelle to digitin.

Digitalinum verum is digitalin Schmiedeberg of the formula $C_{35} H_{56} O_{14}$. (Archiv für Pharmazie 1892, p. 250, 1895, p. 299 and 698, 1899, p. 455 and 458. Berichte der deutschen chemischen Gesellschaft Berlin 1898, p. 2455.)

Digitaliresin is a body formed from digitalin Schmiedeberg by hydrolysis. (Chemisches Zentralblatt 1875, p. 262. Archiv für experimentelle Pathologie, Vol. 3, p. 30 and Vol. 4, p. 191.)

Digitaliretin, $C_{30} H_{25} O_{10}$, is, according to Kosmann, an amorphous body formed by the splitting up of digitalin Kosmann under the action of sulphuric acid; it is only slightly soluble in water, alcohol and ether, but dissolves in hot alcohol. (Journal der pharmacie et de chimie 1860, II, p. 1.—Rochleder, Chemisches Zentralblatt 1863, p. 46.—Schmiedeberg, Archiv für experimentelle Pathologie, Vol. 3, p. 26.) Walz also obtained a digitaliretin by the decomposition of his digitaletin q. v. Neither the preparation of Kosmann nor that of Walz can lay claim to uniformity. (Husemann-Hilger, Pflanzenstoffe, 2nd edition p. 1235.)

Digitaloin is a compound of raw digitalin Walz. (Conf. p. 29.)

Digitalon is the lactone of digitalonic acid. Melting point 138–139° C. The name "digitalon" is also given to a special preparation—a solution of all the glucosides present in digitalis—to be used subcutaneously in doses of 0.5 to 1 c.c. (Pharmazeutische Zeitung 1904, p. 760, Therapie der Gegenwart 1905, p. 398.)

Digitalonic acid, $C_7 H_{14} O_6$, is obtained by the oxidation of digitalose. (Berichte der deutschen chemischen Gesellschaft, Berlin 1892, p. 2116, 1898, p. 2454, 1905, p. 3621, 1909, p. 2610.)

Digitalose is a sugar corresponding to the formula $C_7 H_{14} O_5$, formed together with digitaligenin and grape sugar by the hydrolysis of digitalin Kiliani. (Kiliani, Archiv der Pharmazie 1892, p. 250, 1898, p. 2460.)

Digitalose Homolle-Quevenne is the component of digitalin Homolle which is soluble in a mixture of alcohol and ether, and insoluble in dilute alcohol. (Compare page 29.)

Digitalosmin was the name given by Walz to the odoriferous

principle of Digitalis purpurea; he obtained it by steam distillation from the herb in the form of yellowish-white scales, which glisten like mother-of-pearl, soluble in alcohol or ether and in hot water. They bore a strong smell characteristic of dry digitalis leaves. (Jahrbuch für praktische Pharmazie 1852, Vol. 24, p. 86.)

Digitasolin was the name at first given by Walz to his digitalin. According to Wiggers, however, it is a constituent (compare Roscoe and Schorlemmer, Lehrbuch 1901, VI, p. 682) of (raw) digitalin Walz, which Walz subsequently divided into (what he called) true, pure digitalin, digitalicrin and digitalosin. He gave the melting point of his pure digitalin as 175° C., and the melting point of digitalosin as 137.5° C. (Compare Wiggers, Canstatt's Jahresberichte 1850, Vol. 10, p. 23.)

Digitin Nativelle was described by Nativelle as a crystalline substance, insoluble in water, which possessed neither taste nor physiological action. It was prepared by the author from digitalis leaves and cannot therefore be identified with digitin (Moniteur scientifique 1874, p. 822.)

Digitoflavone is a yellow pigment present in digitalis leaves; it forms crystals and is identical with luteolin. (Fleischer, Dissertation Freiburg 1898. Berichte der deutschen chemischen Gesellschaft Berlin 1899, p. 1184 and 1901, p. 1453.)

Digitogenin is a substance which has the formula $C_{30}H_{48}O_6$, or $C_{30}H_{50}O_6$, formed by hydrolysis from digitonin; it crystallises in fine needles and melts at a temperature above 250° C. Compare page 30. (Archiv. der Pharmazie 1892, p. 261 and 1893, p. 448.—Berichte der deutschen chemischen Gesellschaft Berlin 1890, p. 1555, 1891, p. 339 and 3951, 1899, p. 2201 1901, p. 3562.—Archiv für experimentelle Pathologie, Vol. 3, p. 24.)

Digitogenic acid, according to Kiliani, is an α-ketonic acid, and is formed by the oxidation of digitogenin by means of chromic acid. It is a dibasic acid of the formula $C_{28}H_{44}O_8$. (Berichte der deutschen chemischen Gesellschaft Berlin 1891, p. 343 and 1899, p. 2203.—Archiv der Pharmazie 1893, p. 448 and 1899, p. 466.)

β-Digitogenic acid, $C_{28}H_{44}O_8$, is formed by heating digitogenic acid to 160° C. Colorless crystals melting at 105° C.

(Kiliani, Archiv der Pharmazie 1899, p. 466.—Berichte der deutschen chemischen Gesellschaft Berlin 1899, p. 2205.)

Digitoleinic acid. Kosmann precipitated an aqueous extract of digitalis leaves with lead subacetate and treated the precipitate thus produced by warming with a solution of sodium carbonate. By treating the liquid with sulphuric acid, he was able to precipitate two substances; of these one soluble in ether was called by him digitoleinic acid. It forms a fatty, granular mass. (Journal de connaissance médicale 1845, Vol. 13, Buchner's Repertorium für Pharmazie 1846, Vol. 92, p. 348.)

Digitonein, according to Schmiedeberg, is a body formed by the decomposition of digitonin by means of hydrochloric acid; it is insoluble in ether. (Archiv für experimentelle Pathologie, Vol. 3, p. 22.)

Digitonin, when anhydrous, occurs as an amorphous body, while with $5H_2O$ it is a crystalline, chemically uniform body; its formula is $C_{54}H_{92}O_{28}$ or $C_{54}H_{92}O_{28} + 5H_2O$. (Compare page 30.)

Digitonin, amorphous, is digitonin Schmiedeberg.

Digitonin cryst. is digitonin Kiliani.

Digitonin Kiliani, is pure, crystalline, hydrated digitonin ($C_{54}H_{92}O_{28} + 5H_2O$). Archiv der Pharmazie 1893, p. 460.—Berichte der deutschen chemischen Gesellschaft Berlin 1891, p. 339 and 3951.)

Digitonin Schmiedeberg is amorphous, anhydrous digitonin ($C_{54}H_{92}O_{28}$). According to Kraft, digitonin Schmiedeberg and digitonin Kiliani are not identical; he therefore suggests the designation "digitsaponin" for digitonin Schmiedeberg. (Kraft, Schweizer Wochenschrift für Chemie und Pharmazie 1911, p. 175.)

Digitophyllin, according to Kiliani, is a chemically uniform body with the formula $C_{32}H_{52}O_{10}$. According to Keller, Arnaud and Adrian, it is identical with the French digitaline cristallisée. But neither the identity nor the dissimilarity of these two digitalis products has as yet been conclusively proved. (Archiv der Pharmazie 1897, Vol. 235, p. 426.—van Rijn, The glucosides 1900, p. 425.)

Digitoresin, according to Schmiedeberg, is a substance soluble in ether, formed by treating digitonin with hydrochloric acid.

(Compare above.) (Archiv für experimentelle Pathologie, Vol. 3, p. 22.)

Digitoic acid, $C_{26}H_{42}O_7$, melts at 210° C. It is formed, together with β-digitogenic acid, on heating digitogenic acid to 160° C., or by warming it with solution of caustic potash. (Edinger, Berichte der deutschen chemischen Gesellschaft Berlin 1899, p. 339.—Kiliani, Archiv der Pharmacie 1899, p. 466.—Berichte der deutschen chemischen Gesellschaft Berlin 1899, p. 2201.)

Digitoxigenin, $C_{22}H_{32}O_4$, is a product of decomposition of digitoxin. It is formed, together with a sugar, so-called digitoxose, by the treatment of digitoxin with alcoholic hydrochloric acid at ordinary temperature. Digitoxigenin crystallises in colorless crystals melting at about 230° C. (Archiv der Pharmazie 1895, p. 311 and 1896, p. 481.—Berichte der deutschen chemischen Gesellschaft Berlin 1899, p. 2197.)

Digitoxin (solubile) Cloetta, according to Cloetta, is an amorphous modification of digitoxin, and is only distinguished from the latter by the smaller size of its molecule and its greater solubility in water. Kiliani, however, is of the opinion that digitoxin Cloetta (digalen) is identical with digitalein. (Cloetta, Münchener medizinische Wochenschrift 1904, p. 1466 and 1906, p. 2281.—Kiliani, ibid. 1907, p. 886.—Chemisches Zentralblatt 1907, II, 83.—Merck's Report 1907, p. 88.)

Digitoxin, according to Schmiedeberg and Kiliani, is a chemically uniform substance, which is present in the leaves but not in the seeds of digitalis. Kiliani gave it the formula $C_{34}H_{54}O_{11}$. (Compare above.)

Digitoxin Kiliani
Digitoxin Schmiedeberg } are identical with digitoxin.

β-Digitoxin is digitoxin Kiliani
α-Digitoxin is digitoxin Schmiedeberg } both are identical.

(Archiv der Pharmazie 1895, p. 311 and 1896, p. 277 and 481.)

Digitoxine Pharmacopée française is essentially identical with digitoxin. The French Pharmacopœia requires, inter alia, that the preparation shall give a green color when dissolved in concentrated sulphuric acid, whereas commercial digitoxin gives a brown color on solution. It also requires incorrectly that the preparation shall not dissolve in benzol (benzene). As a matter of fact, however, digitoxin is soluble in benzol (C_6H_6)

and not in petroleum benzin (aether petrolei). The error of the French Pharmacopœia, therefore, is due to the faulty misleading translation of the German " Benzin " into " benzine,' which in French is equivalent to benzol.

Digitoxinic acid, $C_{34}H_{56}O_{12}$, occurs in the form of the sodium salt on heating digitoxin with alcoholic caustic soda. (Kiliani, Archiv der Pharmazie 1899, p. 466.—Berichte der deutschen chemischen Gesellschaft Berlin 1899, p. 2200.)

Digitoxonic acid, $C_6H_{12}O_5$, is obtained by the oxidation of digitoxose. (Berichte der deutschen chemischen Gesellschaft Berlin 1905, p. 4040, 1908, p. 656 and 1909, p. 2610.)

Digitoxose, $C_6H_{12}O_4$, is the sugar formed together with digitoxigenin in the hydrolysis of digitoxin. White crystals melting at 101° C. (Kiliani, Archiv der Pharmazie 1895, p. 311 and 1896, p. 486.—Berichte der deutschen chemischen Gesellschaft Berlin 1898, p. 2455; 1899, p. 2196; 1905, p. 4040.)

Digitsaponin is a designation suggested by Kraft for digitonin Schmiedeberg. (Schweizer Wochenschrift für Chemie und Pharmazie. 1911, p. 175.)

Digitic acid is obtained from digitogenic acid by oxidation with potassium permanganate. It crystallises in needles melting at 192° C., and, according to Kiliani, it has the formula $C_{20}H_{32}O_8$. (Kiliani, Berichte der deutschen chemischen Gesellschaft Berlin 1891, p. 346, and 1899, p. 339.—Archiv der pharmazie 1893, p. 448.)

Digic acid, $C_{16}H_{24}O_6$, is an amorphous acid, which can be obtained by oxidation of the mother-lye of digitic acid. (Kiliani, Archiv der Pharmazie 1894, p. 334.)

Dixgeninic acid, $C_{22}H_{34}O_5$, is obtained in the form of needle shaped crystals, melting at 225° C., by heating digitoxigenin with alcoholic solution of caustic soda. (Kiliani, Berichte der deutschen chemischen Gesellschaft Berlin 1899, p. 2198.)

Gitalin is a glucoside which was obtained by Kraft from digitalis leaves (compare p. 31); it is soluble in 600 parts of cold water. According to Schmiedeberg, it corresponds in strength in its physiological action to digitalinum verum. (Schweizer Wochenschrift für Chemie und Pharmazie 1911, p. 163.)

Gitalin hydrate is, according to Kraft, obtained from gitalin by dissolving the latter in 1½ parts of alcohol at ordinary temperature and adding ¾ of a part of water. It separates in

crystals. (Compare also gitalin p. 31.) . (Schweizer Wochenschrift für Chemie und Pharmazie 1911, p. 162.)

Glucodigitalins was the name given by Ludwig to those preparations of digitalis, which were proved to have the characteristics of glucosides, in contradistinction to acrodigitalins (which see). Archiv der Pharmazie, Vol. 194, p. 213.

Hydrodigitoic acid, $C_{26}H_{44}O_6$, is formed together with digitoic acid by heating digitogenic acid with solution of caustic potash. It softens at 240° C. (Archiv der Pharmazie 1893, p. 457.—Berichte der deutschen chemischen Gesellschaft Berlin 1899, p. 339.)

Oxydigitogenic acid, $C_{28}H_{42}O_9$, is obtained from digitogenin by oxidation with potassium permanganate in alkaline solution. (Kiliani, Berichte der deutschen chemischen Gesellschaft Berlin 1891, p. 345, and 1899, p. 2205.)

Paradigitogenin is formed under special conditions during the hydrolysis of digitonin. (Archiv für experimentelle Pathologie 1875, Vol. 3, p. 25.)

Pseudodigitoxin is the name given by Burmann to a soluble glucoside, similar to gitalin, and obtained from digitalis leaves. (Schweizer Wochenschrift für Chemie und Pharmazie 1911, p. 33.)

Substance cristallisée inerte (Nativelle) is identical with digitin Nativelle.

Toxigenon, $C_{20}H_{26}O_3$ or $C_{19}H_{24}O_3$, is a crystalline body, formed by the oxidation of digitaligenin or of anhydro-digitoxigenin by means of chromic acid; it commences to decompose at 220° C., without melting. (Kiliani, Berichte der deutschen chemischen Gesellschaft Berlin 1898, p. 2459; 1899, p. 2199.)

Toxiresin is, according to Schmiedeberg, a product of decomposition of digitoxin, soluble in ether. (Archiv für experimentelle Pathologie 1875, Vol. 3, p. 39, and Vol. 4, p. 191.)

Various color reactions have been suggested for the chemical identification of the digitalis glucosides; some of these have gained full recognition in laboratory work, but most of them cannot be considered conclusive without the aid of biological tests. The first fairly characteristic reaction was already discovered by Homolle.[17] He found that his digitalin gave an intense green coloration with concentrated hydrochloric acid. To which con-

[17] Homolle, Union médicale 1872, p. 295.

stituent of digitalin Homolle this coloration is due is uncertain; it may, however, be pointed out that among the digitalis glucosides which have since been studied in detail the only one which gives this reaction is digitoxin. Digitalinum verum is colored yellow by hydrochloric acid, digitonin remains colorless and on heating with this acid it becomes red.

Later on Homolle's reaction underwent several modifications, some of which were quite unnecessary, with the intention of rendering it more characteristic. Thus Jorissen [18] used a solution of 1 gramme of zinc chloride in 30 grammes of water and 30 grammes of hydrochloric acid. As might have been expected, it gave a green color with digitalin.[19] The second part of Jorissen's reaction, namely that digitalin when evaporated with the zinc chloride solution mentioned above assumes a brown or black color, cannot be considered characteristic for digitalin, even though Czumpelitz [20] attributes the chestnut-brown color obtained on evaporating to dryness to be due to the condensing action of the zinc chloride. O. Pape [21] varied Homolle's reaction by mixing digitalin [19] with ten times the amount of starch, adding sufficient concentrated sulphuric acid to form a thick paste and then diluting with hydrochloric or nitric acid. The starch is said to be colored green by this method. Lafon [22] heated digitalin [19] with a mixture of alcohol and sulphuric acid (1:1) until it became yellow and then added a drop of very dilute iron chloride solution. This also gave a green color. This color is probably produced by all mineral acids under suitable conditions, and also by sulphuric acid, provided it is not masked by secondary reactions giving dark colored or black products, or by the brown coloration resulting from its mixture with the red digitalin reaction described below. Flückiger [23] modifies the test as follows: he concentrated phosphoric acid (25 p. c.) by heating on a watch glass, and added digitalin Nativelle to the warm acid. The digitalin was colored

[18] Jorissen, Chemisches Zentralblatt 1880, p. 376.

[19] This must be a French digitalin, such as digitalin Homolle, digitalin Nativelle, or digitalin amorph. Gallicum, for digitalinum verum never gives a green coloration.

[20] Czumpelitz, Pharmazeutische Post 1881, p. 47.

[21] Pape, Archiv der Pharmazie, 1876, p. 233.

[22] Lafon, Comptes rendus de l'académie des sciences Vol. 100, p. 1463. — Bulletin de la société chimique Vol. 44, p. 18.

[23] Flückiger, Neues Jahrbuch der Pharmazie Vol. 39, p. 129.

green and the acid yellow. The mechanism of the green coloration has not yet been explained.

While digitoxin produces a green coloration with concentrated hydrochloric acid, it causes a greenish-brown to brown color with concentrated, pure sulphuric acid. Digitalinum verum, on the other hand, is only colored yellow by sulphuric acid. But if the sulphuric acid contains oxidizing substances, such as iron oxide or nitric acid, it yields a deep red color with digitalinum verum. For this reason Grandeau [24] also used bromine with the sulphuric acid for the digitalin reaction, by exposing the solution of digitalin in sulphuric acid to the action of bromine vapor. In carrying out this reaction a violet-red color is obtained. Buckingham [25] used a solution of molybdic acid in sulphuric acid, which yields a crimson color with digitalin. Kiliani [26] describes a digitalin reaction similar to Grandeau's which is probably characteristic of digitalinum verum. If a little digitalinum verum is dissolved in sulphuric acid and a drop of very dilute nitric acid, iron chloride solution, or bromine is added, a bluish-red color is produced, similar to the color of digitalis flowers, which soon disappears. The touch of blue in the red coloration has always been considered of special value.

Keller [27] gives the following reactions for the digitalis glucosides. The glucoside is dissolved in 4 c.c. of glacial acetic acid, one drop of a dilute solution of iron chloride is added and the mixture is layered on to 4 c.c. of sulphuric acid. A colored ring appears at the junction of the liquids. Digitonin gives a pale pink color, which soon disappears. Digitalinum (verum) gives rise to a carmine ring, still plainly visible as a permanent violet-red color if only 0.05 milligramme of digitalin is present in 1 c.c. of glacial acetic acid. Digitalein gives a similar coloration, but it is rather fainter and not so constant. Digitoxin at first gives a dirty greenish-brown color, but very soon the uppermost layer of the sulphuric acid is seen to become brownish-red, while above it a broad, deep bluish-green band is formed, the color of which soon passes into a permanent indigo-blue. While the mechanism of the green color reaction of digitoxin cannot be

[24] Grandeau, Comptes rendus de l'académie des sciences 1864, Vol. 58, p. 1120.
[25] Buckingham, American Journal of Pharmacy 1873, p. 149.
[26] Kiliani, Archiv der Pharmazie, Vol. 230, p. 250.
[27] Keller, Berichte der pharmazeutischen Gesellschaft Berlin 1895, p. 275.

explained, the blue coloration is probably due to the splitting up of the digitoxin, by which digitoxose is formed. This latter most probably causes the blue ring, for Kiliani [28] has found that digitoxose yields a blue color when dissolved in acetic acid containing iron oxide and sulphuric acid.

In analytical practice, the following reaction for the three most important digitalis glucosides have been extensively adopted, being founded on the observations detailed above:

Digitalinum verum (and digitalinum Germanicum) dissolves in pure concentrated hydrochloric acid, or sulphuric acid, giving a yellow color. If a drop of dilute ferric chloride solution is added to the solution in sulphuric acid, a red color containing a touch of blue is immediately produced; the depth of the red coloration varies according to the amount of digitalin present, and it remains constant for days. This coloration is most probably due to digitaligenin, a product of decomposition of digitalin. If sulphuric acid containing iron oxide is used for this reaction, a yellow coloration often appears at first, which lasts for a short time and very soon changes to red. Digitonin is not altered by a similar test; digitoxin is colored a dirty greenish-brown or brown.

Digitoxin is most easily recognized by Keller's reaction described above; it may also be carried out in the following modification. To 100 c.c. of concentrated sulphuric acid about 1 c.c. of a 5 p.c. aqueous solution of ferric sulphate is added, while a mixture of 1 c.c. of the same ferric sulphate solution with 100 c.c. of glacial acetic acid is also prepared. If now a trace of digitoxin is dissolved in about 5 c.c. of this glacial acetic acid containing iron oxide, and this solution is layered on to 5 c.c. of the sulphuric acid containing iron oxide, the coloration, especially the bluish-green band, will become more evident. The green coloration referred to above, formed by the action of concentrated hydrochloric acid on the glucoside, is also characteristic of digitoxin.

Digitonin is not colored either by hydrochloric acid or by sulphuric acid in the cold. On boiling with hydrochloric acid, or with sulphuric acid which is not too dilute, a red solution results the intensity of which gradually increases. (Compare Cloetta, Archiv für experimentelle Pathologie 1901, Vol. 45, p. 435.)

The reactions given above suffice as a means of identification for pharmaceutical purposes; they are not conclusive for forensic

[28] Kiliani, Berichte der deutschen chemischen Gesellschaft Berlin 1898, p. 2454.

purposes. In this case a biological examination is absolutely necessary.

Besides the qualitative tests, the quantitative estimation of digitalis gluocosides in digitalis leaves is of more general interest. So far the estimation of digitoxin, as worked out by Keller, is the only one deserving of consideration. It can be applied in a slightly modified form in the following way.

28 grammes of air-dried, powdered digitalis leaves are placed in a suitable glass-stoppered flask of 500 c.c. capacity; over these are poured 280 grammes of alcohol 60 p.c. (by weight) and the mixture is left to stand for 3 to 4 hours, shaking it frequently. It is then filtered and 207 grammes of the filtrate are evaporated to about 25 grammes on a water-bath. Sufficient water is added to the residue to bring the total weight to 222 grammes, and while stirring, 25 grammes of official liq. plumbi subacetatis fort. are added. The mixture is immediately filtered and to 132 grammes of the filtrate, in an Erlenmeyer flask, a solution of 5 grammes of sodium sulphate in 8 grammes of water is added. When the precipitate has settled, 130 grammes of the clear fluid are poured into a separator, 2 grammes of solution of ammonia (10 p.c. NH_3) are added and the mixture is shaken 5 times, each time with 30 c.c. of chloroform. The chloroformic solutions are filtered and then evaporated, the dry residue is dissolved in 3 grammes of chloroform, and, in order to precipitate the digitoxin, 7 grammes of ether and 50 grammes of petroleum ether are added. The flocculent digitoxin which separates is collected on a small filter (5 cm. diameter) and dissolved on the filter by the addition of hot absolute alcohol. The alcoholic solution which runs through is collected in a glass capsule, evaporated to dryness and the residue dried until the weight is constant. This multiplied by 10 gives the percentage of digitoxin contained in the leaves analysed. But, according to J. Burmann,[29] this so-called digitoxin is pseudodigitoxin, for in contradistinction to true digitoxin it is amorphous and soluble in water and ether. Kraft[30] declares that the product obtained by Keller's method consists chiefly of gitalin (or gitalin hydrate and anhydrogitalin, in addition to digitoxin. He agrees with Burmann in that he also considers Keller's digitoxin to contain only a very small amount of digitoxin.

[29] Burmann, Bulletin de la société chimique 1910, p. 973. — Chemiker-Zeitung 1911, Repert, p. 31.

[30] Kraft, Schweizer Wochenschrift für Chemie und Pharmazie 1911, p. 174.

BOOK REVIEW.

YEAR-BOOK OF PHARMACY AND TRANSACTIONS OF THE PHARMACEUTICAL CONFERENCE, 1912.—This volume of nearly 700 octavo pages comprises abstracts of papers relating to Pharmacy, Materia Medica and Chemistry contributed to British and foreign journals from July 1, 1911, to June 30, 1912, with the transactions of the British Pharmaceutical Conference at the forty-ninth annual meeting held in Edinburgh, July, 1912. The editors and abstractors are to be congratulated on the promptness with which the volume under discussion was published and are to be commended for the completeness and comprehensiveness of the abstracts contained in the nearly 400 pages devoted to this portion of the book.

Following an interesting review of the more important happenings in the sciences related to pharmacy, the abstracts are arranged under the general headings, Chemistry, Materia Medica and Pharmacy, as follows:—Chemistry; alkaloids; animal products; clinical tests; coloring matters; essential oils; fats, fixed oils and waxes; glucosides, sugars, and ferments; gums, oleoresins, and resins; inorganic chemistry; organic chemistry, unclassified; plant analysis: Materia medica; new remedies; pharmacognosy; pharmacology and therapeutics: Pharmacy; dispensing; galenical pharmacy; pharmacopœia revision notes; notes and formulas. This arrangement of the abstracts readily facilitates a critical and comparative study of the progress made in any one branch of pharmaceutical research during the year and also facilitates reference by permitting the juxtaposition of abstracts of closely related articles.

The succinct and yet complete reflection of the transactions of the British Pharmaceutical Conference at its annual meeting, Edinburgh, 1912, is particularly interesting from a practical point of view in that it tends to preserve for future generations of pharmacists an accurate account of the activities of the association.

An index covering 45, double column, pages completes the volume and makes it doubly valuable as a book of reference. Altogether there can be no gainsaying the opinion that the Year-Book for 1912 is a valuable contribution to the literature of pharmacy and that the thanks of pharmacists throughout the English speaking world are due to the members of the British Pharmaceutical Conference particularly for the continuance of this increasingly interesting annual publication. M. I. W.

DR. ALSBERG, THE NEW CHIEF OF THE BUREAU OF CHEMISTRY.

Dr. Carl L. Alsberg, chemical biologist of the Bureau of Plant Industry, U. S. Department of Agriculture, has been appointed chief of the Bureau of Chemistry by President Taft in succession to Dr. Harvey W. Wiley. Dr. Alsberg was born in New York City and is a graduate of Columbia University. He studied abroad at a number of the leading universities, including the University of Berlin, where he did considerable work under Professor Schmiedeburg, the eminent Pharmacologist. Upon his return from Germany he became head of the Department of Biological Chemistry of the Harvard Medical School, and from tnat post entered the Government service. He is a member and ex-Secretary of the Council of Boston Society of Medical Sciences, councillor of the American Chemical Society, Chairman of a section of Biological Chemistry of the American Chemical Society, associate editor of Chemical Abstracts, collaborator of the Journal of Pharmacology and Experimental Therapeutics, and is the author of a long list of scientific papers in both German and English.

In an interview in the *Public Ledger* of December 22, 1912, Dr. Alsberg, while very modest and conservative, yet gives the assurance of recognizing the responsibilities of his position not only to the public but to the manufacturer. He says:

"I believe that most manufacturers and handlers of foodstuffs want to do the right thing, but most of them don't know exactly what is the right thing. The whole subject of food inspection and the demand for pure foods is new. When the Bureau of Chemistry was established there were no standards, no guides of any sort. Everything had to be worked out, and it's been slow work. Only a few things definitely have been determined for this analysis of foods. To establish standards is not the work of days, but of years. When we arrive at what is the standard then we must show the manufacturer how to bring his products up to the standard.

"If we tell a man who is putting up dried fruit that he must not use certain preservatives to prevent the development of insect life in the product, we have gone only half way if we do not show him how he can take care of his fruit in such way as to dispense with the forbidden preservative and still insure the keeping qualities of the product."